

obtaining a parental human cell line capable of producing one or more cytokines; and
modifying cells of said parental cell line by introducing a first expression vector
comprising: (i) the coding sequence for CrmA operably linked to a first promoter, and (ii)
additional control elements necessary for expression in human cells, into the cells of said cell
line; and

screening and selecting for CrmA-expressing cells.

4. (Amended) The human cell line according to claim 3, wherein the process further
comprising:

treating said CrmA-expressing cells in a manner effective to result in enhanced cytokine
production, wherein said modified and treated cell line is characterized by a level of cytokine
production that is at least two times (2X) the level of cytokine production by the corresponding
non-transformed parental cell line.

5. (Amended) The human cell line according to claim 3, wherein the process further
comprising:

modifying cells of said parental cell line by introducing a second expression vector
comprising: (i) the coding sequence for PKR operably linked to a second promoter; and (ii)
additional control elements necessary for expression in human cells, into the cells of said cell
line, wherein said introduction of said first expression vector to said cells is prior, at the same time
or after said introduction of said second expression vector to said cells; and
screening and selecting for PKR overexpressing cells.

6. (Amended) The human cell line according to claim 5, wherein the process further
comprising:

treating said CrmA and PKR over expressing cells of said human cell line in a manner
effective to result in enhanced cytokine production, wherein said modified and treated cell line is
characterized by a level of cytokine production that is at least two times (2X) the level of
cytokine production by the corresponding not-modified parental cell line.

7. (Amended) The human cell line according to claim 6, wherein treating means
subjecting said modified cells to one or both of priming and inducing.

8. (Amended) The human cell line according to claim 7, wherein priming means exposing said modified cells to phorbol myristate acetate (PMA) or interferon- β .

9. (Amended) The human cell line according to claim 7, wherein inducing means exposing said modified cells to a microbial inducing agent selected from the group consisting of Sendai virus, encephalomyocarditis virus and Herpes simplex virus.

10. (Amended) The human cell line according to claim 9, wherein said microbial inducing agent is Sendai virus.

11. (Amended) The human cell line according to claim 7, wherein inducing means exposing said cells to at least one non-microbial inducing agent selected from the group consisting of poly(I):poly(C) (poly IC), or poly r(I):poly r(C) (poly rIC), heparin, dextran sulfate, cycloheximide, Actinomycin D, sodium butyrate, a calcium ionophore and chondroitin sulfate.

12. (Amended) The human cell line according to claim 11, wherein inducing means exposing said cells to polyI:C, cycloheximide and Actinomycin D.

13. (Amended) In an improved method for producing one or more cytokines in human cell culture, the improvement directed to increasing cell viability and the amount of cytokine production, by culturing a parental human cell line under conditions of one or more of (i) modification effective to result in anti-apoptotic protein expression; (ii) modification effective to result in cytokine regulatory factor overexpression; (iii) priming; and (iv) inducing, wherein the amount of cytokine production is at least two times (2X) the level of cytokine production by the corresponding non-modified parental cell line.

14. (Amended) The method according to claim 13, wherein modification effective to result in anti-apoptotic protein expression means introducing a first expression vector comprising: (i) the coding sequence for CrmA operably linked to a first promoter, and (ii) additional control elements necessary for expression of CrmA in human cells into the cells of said cell line; and screening and selecting for CrmA-expressing cells.

15. (Amended) The method according to claim 13, wherein modification effective to result in cytokine regulatory factor overexpression means introducing a second expression vector

comprising: (i) the coding sequence for PKR operably linked to a second promoter, and (ii) additional control elements necessary for expression of PKR in human cells into cells of said cell line, wherein said introduction of said first expression vector to said cells is prior, at the same time, or after said introduction of said second expression vector to said cells; and screening and selecting for PKR-overexpressing cells.

16. (Amended) The method according to claim 13, wherein priming means exposing cells of said cell line to one or both of phorbol myristate acetate (PMA) and interferon- β .

17. (Amended) The method according to claim 13, wherein inducing means exposing cells of said cell line to a microbial inducing agent selected from the group consisting of Sendai virus, encephalomyocarditis virus and Herpes simplex virus.

18. (Amended) The method according to claim 13, wherein inducing means exposing cells of said cell line to at least one non-microbial inducing agent selected from the group consisting of poly(I):poly(C) (poly IC), or poly r(I):poly r(C) (poly rIC), heparin, dextran sulfate, cycloheximide, Actinomycin D, sodium butyrate, a calcium ionophore and chondroitin sulfate.

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19. (Amended) The method according to claim 13, wherein the one or more cytokine(s) are selected from the group consisting of interferon-alpha (IFN-alpha), interferon-beta (IFN-beta), interferon-gamma (IFN-gamma); granulocyte macrophage colony stimulating factor (GM-CSF); granulocyte colony stimulating factor (G-CSF); interleukin-2 (IL-2); interleukin-3 (IL-3); interleukin-7 (IL-7); interleukin-8 (IL-8); interleukin-10 (IL-10); and interleukin-12 (IL-12).

Please add the following new claims:

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20. The method according to claim 17, wherein said microbial inducing agent is Sendai virus.

21. The method according to claim 18, wherein said non-microbial inducing agent are polyI:C, cycloheximide and Actinomycin D.

22. The method according to claim 14, wherein said first expression vector further comprises a first selectable marker encoding nucleic acid sequence; and wherein said screening

and selecting for CrmA-expression cells mean culturing said modified cells in medium containing a first selection agent to select for CrmA-expressing cells.

23. The method according to claim 15, wherein said second expression vector further comprises a second selectable marker encoding nucleic acid sequence; and wherein said screening and selecting for PKR overexpressing cells mean culturing said modified cells in medium containing a second selection agent to select for PKR overexpressing cells.

24. The method according to claim 14, wherein said parental human cell line is also capable of expressing PKR, and wherein modification effective to result in cytokine regulatory factor overexpression comprises screening and selecting for PKR overexpressing cells that exhibits at least a 2-fold (2X) increase in PKR activity, expression and/or production.

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25. The human cell line according to claim 4, wherein treating means subjecting said modified cells to one or both of priming and inducing.

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26. The human cell line according to claim 25, wherein priming means exposing said modified cells to phorbol myristate acetate (PMA) or interferon- β .

27. The human cell line according to claim 25, wherein inducing means exposing said modified cells to a microbial inducing agent selected from the group consisting of Sendai virus, encephalomyocarditis virus and Herpes simplex virus.

28. The human cell line according to claim 27, wherein said microbial inducing agent is Sendai virus.

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29. The human cell line according to claim 25, wherein inducing means exposing said cells to at least one non-microbial inducing agent selected from the group consisting of poly(I):poly(C) (poly IC), or poly r(I):poly r(C) (poly rIC), heparin, dextran sulfate, cycloheximide, Actinomycin D, sodium butyrate, a calcium ionophore and chondroitin sulfate.

30. The human cell line according to claim 29, wherein inducing means exposing said cells to polyI:C, cycloheximide and Actinomycin D.

31. The human cell line according to claim 3, wherein said parental human cell line is also capable of expressing PKR, and wherein the process further comprises screening and selecting for PKR overexpressing cells that exhibit at least a 2-fold (2X) increase in PKR activity, expression and/or production.

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32. The human cell line according to claim 31, wherein the process further comprising: treating said PKR overexpressing cells in a manner effective to result in enhanced cytokine production, wherein said modified and treated cell line is characterized by a level of cytokine production that is at least two times (2X) the level of cytokine production by the corresponding not-modified parental cell line.

33. The human cell line according to claim 32, wherein treating means subjecting said modified cells to one or both of priming and inducing.

~~Sub B5~~ 34. The human cell line according to claim 33, wherein priming means exposing said modified cells to phorbol myristate acetate (PMA) or interferon- β .

35. The human cell line according to claim 33, wherein inducing means exposing said modified cells to a microbial inducing agent selected from the group consisting of Sendai virus, encephalomyocarditis virus and Herpes simplex virus.

36. The human cell line according to claim 35, wherein said microbial inducing agent is Sendai virus.

~~Sub B6~~ 37. The human cell line according to claim 33, wherein inducing means exposing said cells to at least one non-microbial inducing agent selected from the group consisting of poly(I):poly(C) (poly IC), or poly r(I):poly r(C) (poly rIC), heparin, dextran sulfate, cycloheximide, Actinomycin D, sodium butyrate, a calcium ionophore and chondroitin sulfate.

R2 38. The human cell line according to claim 37, wherein inducing means exposing said cells to polyI:C, cycloheximide and Actinomycin D.

~~Sub C1~~ 39. The human cell line according to claim 3, wherein said first expression vector further comprises a first selectable marker encoding nucleic acid sequence; and wherein said screening

and selecting for CrmA-expression cells mean culturing said modified cells in medium containing a first selection agent to select for CrmA-expressing cells.

40. The human cell line according to claim 5, wherein said second expression vector further comprises a second selectable marker encoding nucleic acid sequence; and wherein said screening and selecting for PKR overexpressing cells mean culturing said modified cells in medium containing a second selection agent to select for PKR overexpressing cells.

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